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ANDRUS, SCEALES, STARKE & SAWALL, LLP
100 EAST WISCONSIN AVENUE, SUITE 1100
MILWAUKEE, WI 53202

EXAMINER	
REIDEL, JESSICA L	

ART UNIT	PAPER NUMBER
3766	

DATE MAILED: 04/07/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/824,950	XUE ET AL.	
	Examiner	Art Unit	
	Jessica L. Reidel	3766	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 January 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 April 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03/09/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Acknowledgement is made of Applicant's Amendment, which was received by the Office on January 30, 2006. Claim 20 has been cancelled. Claims 1-19 are pending.

Information Disclosure Statement

2. The information disclosure statement (IDS) submitted on March 9, 2006 has been acknowledged and is being considered by the Examiner.

Specification

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

The following title is suggested: "Methods for analysis of non-invasive cardiac parameters".

Claim Objections

4. Claim 1 is objected to because of the following informalities: there appears to be a typographical error in the third line of the claim. The Examiner suggests changing "the patient's" to "a patient's" to avoid an antecedent basis problem. Appropriate correction is required.

Claim Rejections - 35 USC § 101

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claim 1 is rejected under 35 U.S.C. 101 because the claimed invention lacks patentable utility. The last line of Claim 1 recites the limitation "analyzing variation between the first value and the second value", which appears to be an abstract idea rather than a practical application of

that idea. The Examiner suggests adding a tangible, useful and concrete method step wherein the method employs the "analyzing" by "performing an action" or "completing a method step". An example suggestion is incorporation of the limitation presented in Claim 2 to add utility to the independent Claim 1 such as modifying Claim 1 as follows: "analyzing a variation between the first value and the second value by defining the relationship between depolarization and repolarization to include a QRS-T angle".

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1-3 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Anderson (U.S. 4,136,690). As to Claims 1 and 2, Anderson discloses a method using an electrocardiogram (ECG) signal comprising measuring a QRS-T angle, read as defining a relationship, between the QRS peak vector, read as depolarization, and the T-wave peak vector, read as repolarization. Anderson discloses that the QRS-T angle is "successively stored" and the Examiner interprets this to mean that the QRS-T angle is determined for a first beat of the ECG, a second beat of the ECG and successive beats of the ECG (see Anderson column 2, lines 19-50 and column 3, lines 8-64). Anderson further discloses that each stored QRS-T angle is tallied into one of a number of angular ranges for

analysis and comparison between ranges (see Anderson column 3, lines 57-67, column 7, lines 43-47 and column 8, lines 59-66). It is inherent or at least obvious to one having ordinary skill in the art at the time the invention was made that, although not expressly disclosed by Anderson, the accumulated data stored, displayed or printed and used for analysis in the method of Anderson assesses a patient's cardiac vulnerability to sudden cardiac death because any arrhythmias present in the vectorcardiograph can be detected and classified and arrhythmias are a well known precursor to sudden cardiac death. The Examiner takes the position that a method, which classifies arrhythmias present in a patient's ECG signal, inherently assesses "vulnerability" to "sudden cardiac death" since an arrhythmia present in a patient's ECG indicates that a patient is more "vulnerable" to experiencing "sudden cardiac death".

9. As to Claim 3, Anderson discloses that it is well known in the art to obtain a medically-significant vector electrocardiogram through the use of a three-lead system such as the Frank lead system or the modified McFee lead system (see Anderson column 1, lines 11-33).

10. Claims 1, 4-5 and 8 are rejected under 35 U.S.C. 102(e) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Burnes (U.S. 2004/0220635). As to Claim 1, Burnes discloses a method using an ECG comprising determining an activation recovery interval (ARI), read as a relationship, as the difference between activation time, read as depolarization, and recovery time, read as repolarization (see Burnes page 8, Claim 6). Burnes also discloses that if a subsequent comparison of a prior dispersion of ARI reveals an increased dispersion of ARI, a worsening heart failure condition is declared (see Burnes page 5, paragraphs 48-51). It is inherent that the subsequent ARI is determined for a first beat and the prior dispersion of ARI determined for a second beat. It is inherent or at least obvious to one having ordinary skill in the

art at the time the invention was made that, although not expressly disclosed by Burnes, the detection of increased dispersion disclosed is capable of assessing a patient's cardiac vulnerability to sudden cardiac death because the method indicates a worsening of heart failure and/or increased risk of arrhythmias, both precursors and/or indicators of sudden cardiac death. In addition the detection of increased dispersion disclosed by Burnes is inherently indicative of an increased "vulnerability" to "sudden cardiac death".

11. As to Claims 4 and 5, Burnes discloses that determination of the dispersion of the ARI includes QRS duration and QT duration and QRS duration and T duration (see Burnes page 1, paragraphs 3-5 and page 6, paragraphs 53-55).

12. As to Claim 8, Bunres also discloses that dispersion measurements may be performed on a periodic basis for monitoring heart failure status, monitoring arrhythmia risk, or optimizing a therapy in order to reduce dispersion, for example by adjusting cardiac pacing parameters during CRT or adjusting the dosage of a drug therapy (see Burnes page 5, paragraph 47). It is inherent the such an optimization would include selecting a first beat from an ECG signal obtained from the patient prior to the event and selecting the second beat from an ECG signal obtained from the patient after the event. It is also inherent that a first beat selected in this manner would be from an ECG having a heart rate within a first range and a second beat selected in this manner would be from an ECG having a heart rate within a second range that is different from the first due to the administered therapy.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson. Anderson discloses the claimed invention except the method does not specify selecting the first beat and the second beat from median beats or mean beats. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method as taught by Anderson to include selecting the first beat and the second beat from median or mean beats since it was known in the art that such a statistical selection method is used to provide means for lessening the affect that spurious signals have on the diagnosis results.

15. Claims 9 and 18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Kaplan et al. (U.S. 4,732,157) (herein Kaplan). Anderson discloses the claimed invention as discussed above except that the method does not further comprise conduction a time series analysis of the first and second values.

Kaplan, however, teaches that is known to use a time series to quantify beat-to-beat variability in an ECG waveform in order to determine susceptibility to ventricular fibrillation (see Kaplan column 5, lines 12-23 and column 6, lines 1-22). Kaplan also discloses that an objective of the time series analysis on a plurality of beats is to derive a numerical parameter from the ECG, which is associated with susceptibility to ventricular fibrillation (see Kaplan Abstract and column 2, lines 25-30). Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Anderson in view of Kaplan to include a time series analysis in order to derive a numerical parameter associated with susceptibility to ventricular fibrillation.

16. Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Verrier et al. (U.S. 5,265,617) (herein Verrier '617). Anderson discloses the claimed invention as discussed above except that the method does not further comprise using a cardiac parameter or heart rate variability in addition to the ECG signal to asses the patient's cardiac vulnerability to sudden cardiac death.

Verrier '617, however, discloses a method and apparatus for the non-invasive diagnosing of cardiac vulnerability to ventricular fibrillation that comprises evaluating heart rate variability in addition to T-wave alternans of the ECG signal (see Verrier '617 Title and Abstract). Verrier '617 discloses that heart rate variability is a measure of autonomic influence, which is a major factor in triggering cardiac arrythmias and that by simultaneous analysis of the ECG signal and heart rate variability allows for the extent and cause of cardiac vulnerability to be assessed so that drug therapy may be tailored per patient (see Verrier '617 column 4, lines 54-67 and column 5, lines 1-5). The Examiner takes the position that heart rate variability is synonymous with a cardiac parameter. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Anderson in view of Verrier '617 to include simultaneous evaluation of heart rate variability in addition to the ECG signal to better asses the patient's vulnerability to sudden cardiac death and to tailor a drug therapy as best to treat the patient.

17. Claims 12 and 14-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Ralph et al "Blunted arterial baroreflec causes 'pathological' heart rate turbulence", cited by Applicant (herein Ralph). Anderson discloses the claimed invention as

discussed above except that the method does not further comprise using heart rate turbulence in addition to the EC signal.

Ralph, however, teaches that it is known to utilize a characteristic of baroreflex function such as heart rate turbulence (either onset or slope) as set forth in the Abstract and the third paragraph on page 2, as a superior predictor of sudden cardiac death. In particular, Ralph discloses that turbulence onset is defined prior to a premature ventricular contraction and after the premature ventricular contraction and turbulence slope is defined within the first 20 sinus-rhythm intervals after the premature contraction. The Examiner takes the position that PVCs naturally have varying cycle lengths and varying morphologies. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method as taught by Anderson, to include heart rate turbulence in addition to analysis of the ECG signal as taught by Ralph, since such a modification would provide a substantial improvement in the ability to predict sudden cardiac death.

18. Claim 13 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Ralph and Verrier et al. (U.S. 5,560,370) (herein Verrier '370). The previously modified Anderson reference discloses the claimed invention as discussed above except that the method does not comprise using data corresponding to blood pressure change in addition to heart rate turbulence to asses the patient's cardiac vulnerability to sudden cardiac death.

Verrier '370, however, discloses a method for prediction of cardiac electrical instability that uses baroreflex sensitivity as an additional indicator of cardiac electrical instability and that this sensitivity may be non-invasively characterized as blood pressure (see Verrier '370 column 20, lines 34-45). It would have been obvious to one having ordinary skill in the art to modify the

method of Anderson in view of Ralph and Verrier to include using data corresponding to blood pressure in addition to heart rate turbulence to non-invasively asses the patient's cardiac vulnerability to sudden cardiac death.

19. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Ralph and Burnes. The previously modified Anderson reference discloses the claimed invention except that selecting the first beat from an electrocardiogram signal obtained from the patient is not disclosed to occur prior to an event and selecting the second beat from an electrocardiogram signal obtained from the patient is not disclosed to occur at least one of during and after the event where the event includes at least one of administering a pharmaceutical drug to a patient, pacing the patient using exercise, and pacing the patient using an implanted pacemaker.

Burnes, however, discloses a method using an ECG comprising determining an activation recovery interval (ARI), read as a relationship, as the difference between activation time, read as depolarization, and recovery time, read as repolarization (see Burnes page 8, Claim 6). Burnes also discloses that if a subsequent comparison of a prior dispersion of ARI reveals an increased dispersion of ARI, a worsening heart failure condition is declared (see Burnes page 5, paragraphs 48-51). It is inherent that the subsequent ARI is determined for a first beat and the prior dispersion of ARI determined for a second beat. In addition the detection of increased dispersion disclosed by Burnes is capable of assessing a patient's cardiac vulnerability to sudden cardiac death because the method indicates a worsening of heart failure and/or increased risk of arrhythmias, both precursors and/or indicators of sudden cardiac death. Bunres also discloses that dispersion measurements may be performed on a periodic basis for monitoring heart failure

status, monitoring arrhythmia risk, or optimizing a therapy in order to reduce dispersion, for example by adjusting cardiac pacing parameters during CRT or adjusting the dosage of a drug therapy (see Burnes page 5, paragraph 47). It is inherent the such an optimization would include selecting a first beat from an ECG signal obtained from the patient prior to the event and selecting the second beat from an ECG signal obtained from the patient after the event. It would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method as taught by Anderson in view of Ralph and Burnes to include a step of selecting the first beat from an ECG obtained from the patient prior to an event and selecting the second beat from an ECG obtained from the patient after the event where the event includes administering a pharmaceutical drug to a patient in order optimize the invention.

20. Claim 19 is rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson in view of Kaplan and Verrier '617. The previously modified Anderson reference discloses the claimed invention as discussed above except that the method does not further comprise using a cardiac parameter or heart rate variability in addition to the ECG signal to asses the patient's cardiac vulnerability to sudden cardiac death.

Verrier '617, however, discloses a method and apparatus for the non-invasive diagnosing of cardiac vulnerability to ventricular fibrillation that comprises evaluating heart rate variability in addition to T-wave alternans of the ECG signal (see Verrier '617 Title and Abstract). Verrier '617 discloses that heart rate variability is a measure of autonomic influence, which is a major factor in triggering cardiac arrythmias and that by simultaneous analysis of the ECG signal and heart rate variability allows for the extent and cause of cardiac vulnerability to be assessed so that drug therapy may be tailored per patient (see Verrier '617 column 4, lines 54-67 and column

5, lines 1-5). The Examiner takes the position that heart rate variability is synonymous with a cardiac parameter. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the method of Anderson in view of Kaplan and Verrier '617 to include simultaneous evaluation of heart rate variability in addition to the ECG signal to better asses the patient's vulnerability to sudden cardiac death and to tailor a drug therapy as best to treat the patient.

Response to Arguments

21. Applicant's arguments filed January 30, 2006 have been fully considered but they are not persuasive. In regards to Applicant's statement at page 7, lines 17-18 that the Examiner stated in the Office Action of November 9, 2005 that Anderson and Burnes "fail to teach or suggest such a method" the Examiner feels that this is incorrect and would like to bring the Applicant's attention to the tops of both pages 3 and 4 of the Office Action of November 9, 2005. To clarify, although Anderson and Burnes do not *expressly disclose* that the methods are used to assess a patient's cardiac vulnerability to sudden cardiac death, both methods *inherently perform as such methods and are capable of assessing a patient's vulnerability to sudden cardiac death.* For instance, Anderson provides a method for detecting and classifying arrhythmias present in a vectocardiograph. It is well known in the art that a patient experiencing an arrhythmia would have a higher vulnerability to sudden cardiac death than a patient that experiences no arrhythmias, thus the method inherently assesses a patient's cardiac vulnerability to sudden cardiac death. Also, Burnes provides a method that indicates a worsening of heart failure, and/or increased risk of arrhythmias. It is well known in the art that a patient experiencing worsening heart failure would have a lower mortality and higher vulnerability to sudden cardiac death and a

patient experiencing a higher risk of arrhythmia would consequently have a higher vulnerability to sudden cardiac death, thus the method inherently assesses a patient's cardiac vulnerability to sudden cardiac death.

Conclusion

22. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Kupper (U.S. 2003/0014083) discloses a method and apparatus which evaluates heart operation and modifies administered therapy based upon a correlation between atrial cycle time, read as depolarization of the heart and ventricular cycle time, read as repolarization of the heart.

Malik et al. (U.S. 6,438,409) herein Malik teaches that it is well known in the art to utilize a relationship between depolarization and repolarization as a predictor for mortality in patient's who have suffered acute myocardial infarction and as a predictor for arrhythmias – both well known in the art as precursors of sudden cardiac death.

23. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica L. Reidel whose telephone number is (571) 272-2129. The examiner can normally be reached on Monday-Thursday 8:00-5:30, every other Friday 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Robert Pezzuto can be reached on (571) 272-6996. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jessica L. Reidel 04/03/06
Examiner
Art Unit 3766

Robert E. Pezzuto
Supervisory Patent Examiner
Art Unit 3766